European Spine Journal (2021) 30:3428–3441
https://doi.org/10.1007/s00586-021-06990-2

REVIEW ARTICLE

Paraspinal muscle imaging measurements for common spinal disorders: review and consensus-based recommendations from the ISSLS degenerative spinal phenotypes group

Paul W. Hodges[1] · Jeannie F. Bailey[2] · Maryse Fortin[3] · Michele C. Battié[4]

Received: 9 July 2021 / Revised: 12 August 2021 / Accepted: 5 September 2021 / Published online: 20 September 2021

Abstract

Purpose Paraspinal muscle imaging is of growing interest related to improved phenotyping, prognosis, and treatment of common spinal disorders. We reviewed issues related to paraspinal muscle imaging measurement that contribute to inconsistent findings between studies and impede understanding.

Methods Three key contributors to inconsistencies among studies of paraspinal muscle imaging measurements were reviewed: failure to consider possible mechanisms underlying changes in paraspinal muscles, lack of control of confounding factors, and variations in spinal muscle imaging modalities and measurement protocols. Recommendations are provided to address these issues to improve the quality and coherence of future research.

Results Possible pathophysiological responses of paraspinal muscle to various common spinal disorders in acute or chronic phases are often overlooked, yet have important implications for the timing, distribution, and nature of changes in paraspinal muscle. These considerations, as well as adjustment for possible confounding factors, such as sex, age, and physical activity must be considered when planning and interpreting paraspinal muscle measurements in studies of spinal conditions. Adoption of standardised imaging measurement protocols for paraspinal muscle morphology and composition, considering the strengths and limitations of various imaging modalities, is critically important to interpretation and synthesis of research.

Conclusion Study designs that consider physiological and pathophysiological responses of muscle, adjust for possible confounding factors, and use common, standardised measures are needed to advance knowledge of the determinants of variations or changes in paraspinal muscle and their influence on spinal health.

Keywords Imaging · Paraspinal muscles · Multifidus · Magnetic Resonance Imaging · Ultrasound

Introduction

There is growing interest to improve the contribution of phenotyping based on paraspinal muscle imaging to the prognosis and treatment guidance of common spinal conditions. Recent reviews have investigated the association between imaging-based spinal muscle phenotypes and spinal disorders, including non-specific low back pain (LBP), neurocompressive conditions, and physical function in older adults [1–6], but findings are conflicting and inconclusive.

Beyond differences between study samples, inconsistent results between studies have several possible methodological explanations, including different approaches to paraspinal muscle measurements and variable control of confounding factors. Such methodological variations limit study comparisons and meta-analyses and have led to calls for the adoption of uniform measurement techniques [1, 3, 7]. Further, study design and interpretation require consideration of the physiological mechanisms associated with changes in spinal muscles. These differ between spinal conditions and can affect the distribution, timing, and nature of muscle changes

✉ Paul W. Hodges
p.hodges@uq.edu.au

1 School of Health and Rehabilitation Sciences, The University of Queensland, Brisbane, QLD 4072, Australia

2 Department of Orthopedic Surgery, University of California, San Francisco, CA, USA

3 Department of Health, Kinesiology & Applied Physiology, Concordia University, Montreal, QC, Canada

4 Faculty of Health Sciences and Western's Bone and Joint Institute, Western University, London, ON, Canada

and require careful consideration when selecting appropriate measurement sites and measures.

Refinement of study design and measures will be necessary to advance knowledge of the determinants of variation or changes in paraspinal muscle and their influence on back health and function. Towards this goal, this paper reviews three key sources of inconsistencies among studies of paraspinal muscle measurements in spinal conditions (excluding neuromuscular disorder/muscular dystrophies) that require attention, including the failure to: (1) consider possible mechanisms underlying changes in paraspinal muscles; (2) control for confounding factors; and (3) standardise spinal muscle imaging modalities and protocols for measurement of muscle size, composition, and asymmetry.

Physiology and pathophysiology of paraspinal muscle changes with LBP and other spine conditions

Interpretation of muscle imaging requires an understanding of the possible mechanisms underlying muscle changes with LBP, as these mechanisms influence the *distribution, timing,* and *nature* of any changes (Table 1). Recent animal and human studies have begun to unravel some of the complexities. Much of the work focuses on the multifidus muscle.

An understanding of the distribution of paraspinal muscle changes requires consideration of muscle anatomy and innervation. Multifidus, in which there is particular interest, arises from the spinous process, lamina, and mammillary process of the lumbar vertebrae (Fig. 1). The deep fascicles descend over two lumbar intervertebral segments. More superficial fascicles cross up to five segments [8]. All fibres arising from a spinal segment are innervated by that level's nerve root [8]. Thus, single-level denervation could influence fascicle bundles within the muscle's cross-sectional area up to 5 levels below. Findings localised to a single level would likely involve the deeper short muscle fascicles. Findings at multiple levels could be mediated by changes to long fascicles that arise from a single segment, or from mechanisms that affect multiple levels simultaneously (e.g., disuse).

Pathophysiology of multifidus muscle changes in LBP, pathology, and injury

Neural mechanisms

Several neural mechanisms have been proposed, each with different implications for the distribution, timing, and nature of changes (Table 1; Fig. 1).

Reflex inhibition (inhibition of motoneurones mediated by afferent input from joint injury) has been extensively studied in peripheral joints (e.g., knee). It particularly involves extensor muscles [9] at a single spinal segment [10]. Effects can be prolonged (> 2 weeks) [11] and can occur in the absence of pain [12]. Immediately after intervertebral disc (IVD) injury in animals, the response of multifidus to electrical stimulation at the spinal cord is reduced but increased to motor cortex stimulation. Together these observations imply reflex inhibition at a spinal level [13]. Animal experiments highlight a bias to inhibition of deep fascicles of multifidus [13], which explains localised acute muscle atrophy in humans [14] and animals [15](Fig. 1).

Denervation results from motor axon compression/damage secondary to neurocompressive conditions of the intervertebral foramen or spinal canal, such as spinal stenosis [16] and IVD herniation [17], or iatrogenically from radiofrequency ablation of the dorsal ramus which provides sensory innervation to the facet joint in addition to motor innervation to multifidus. It is segmental and specific [18] and causes metabolic and morphological muscle changes (e.g. atrophy) leading to replacement of muscle with fat and connective tissue [19]. Denervation is demonstrated by reduced neural drive [20] and histological evidence of reinnervation of muscle fibres (e.g. clusters of muscle fibres of the same type caused by sprouting to reinnervate fibres [21]). Because all fibres of multifidus arising from a vertebra are innervated by the spinal nerve root from that level [8], denervation would induce muscle changes over multiple levels, on the side of the nerve root. This distribution occurs after nerve transection in animals [15]. Over time, if reinnervation occurs, changes can resolve [20]. In non-spinal musculoskeletal complaints, distribution of fat and atrophy can differ between muscle changes mediated by denervation and disuse [22]. Denervation-induced muscle changes may occur along with pain but are not caused by pain.

Modified motor control involves altered functioning of spinal/supraspinal sensorimotor circuits. Individuals with chronic and recurrent LBP have a variety of changes in back muscle activation that depend on the patient, time course, and task, with reduced or delayed multifidus activation being common [23, 24]. Some differences relate to posture [25] or movement [26], and neurophysiological features, such as organisation of the muscle's representation on the motor cortex [27] and modified brain inhibitory/excitatory mechanisms [28]. Changes differ between individuals, may be specific to subgroups with specific clinical features [25], and can be localised or diffuse. In acute LBP, multifidus activation can be decreased [29] or increased [30]. Changes in other paraspinal muscles are also variable [31].

Table 1 Features of muscle imaging expected with discrete physiological mechanisms for muscle changes in back pain and injury

Mechanism	Definition	Example conditions	Outcomes	Imaging findings	Distribution	Time course
Reflex inhibition	Inhibition of motoneurones mediated by afferent input from injury or loading of joint tissues	Expected in the acute phase with any injury	Atrophy; reduced activation of muscle at a single segment; reduced spinal motoneurone excitability	Atrophy	Identified at a single segment on one side. As fibres innervated by a spinal nerve root pass caudally from the vertebrae, the greatest change would be expected adjacent to spinous process one segment below	Begins within 3 days, thought to last up to 2 weeks
Denervation	Loss of sensory/motor innervation secondary to neuro-compression or nerve injury	Spinal stenosis, IVD herniation	Atrophy, changes in muscle fibre distribution, fat infiltration	Atrophy, fat infiltration	Changes would impact all fascicles innervated by the affected nerve root. These would cross up to 5 levels and be observed in only a portion of the cross section of the muscle in a transverse image, as this includes overlapping fascicles innervated by different levels	Fat accumulation over months; might recover if muscle is reinnervated
Modified motor control	Altered drive to muscles as a result of altered functioning of spinal/supraspinal sensorimotor circuits secondary to pain/injury/ threat of pain/injury	Possible with any presentation of pain/injury or threat of pain/injury	Highly variable	Atrophy, hypertrophy, fat infiltration	Highly variable depending on the individual, could be multiple levels, unilateral or bilateral	Highly variable
Disuse/ unloading	Decreased neural drive to muscle or decreased load on muscle	Micro-gravity, rest/ inactivity, movement patterns that unload specific muscle groups	Atrophy that is unevenly distributed between muscles (e.g., multifidus > erector spinae)	Atrophy	Multiple levels involved; bilateral or unilateral (depending on nature of unloading/ disuse)	Can commence early; extent of changes depends on duration of disuse
Inflammatory mechanisms	Muscle structural changes secondary to local inflammatory response (TNF; IL-1β)	Shown in IVD disease/ injury but possible in other conditions	Atrophy; slow-to-fast muscle fibre-type changes; fat infiltration; fibrosis	Atrophy; fat infiltration	Initial changes are localised (single level/single side). Distribution becomes more diffuse over time	3–6 months after injury; more extensive over time

TNF—Tumour necrosis factor; IL-1β—interleukin 1-beta; IVD—intervertebral disc

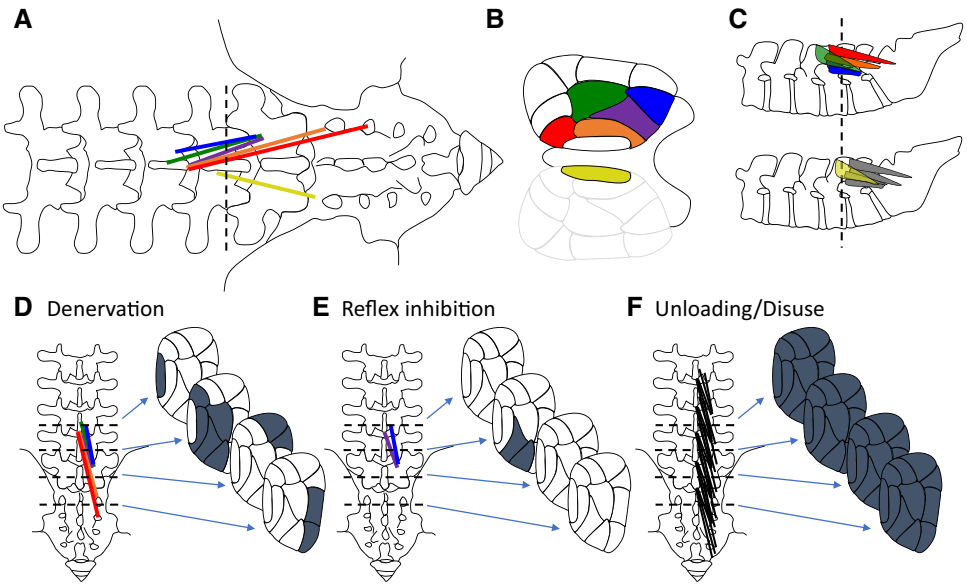

Fig. 1 Anatomy of the multifidus muscle and distribution of muscle changes with different mechanisms for dysfunction. **(a)**. Anatomy of fascicles of the multifidus muscle arising from the spinous process and lamina of L3 is shown on the right side of the spine (top). The left (bottom) shows a fascicle bundle that arises from the side of the spinous process of L4. Fibres cross 2–5 segments. All fascicles arising from L3 are innervated by the spinal nerve root of the same number. **(b)**. Cross section of multifidus through the middle of the L4 spinous process. Colours identify the same fibres as shown in panel A and C. Note the fascicle bundle closest to the spinous process (yellow) arises from the from the side of the L4 spinous process, whereas all other coloured fascicles arise from L3. **(c)**. Top shows all fascicles from L3, and bottom shows all fascicles from L4. **(d)**. Expected distribution of muscle changes from denervation of the L3 nerve root (shown in grey). Atrophy will be expected to involve all muscle fascicles arising from L3, which occupy different locations in the cross-sectional view at each level. E. Expected distribution of muscle changes from reflex inhibition involving the L3 spinal level (shown in grey). Evidence suggests most involvement of the shortest fibres with muscle bulk at a single level. F. Expected distribution of muscle changes from unloading/disuse. This would be expected to be generalised and involve all muscle fascicles (shown in grey)

Disuse/muscle unloading mechanisms

Disuse induces muscle structural change including atrophy [32–34] and fat accumulation [35]. Reduced muscle loading/stretch upregulates adipogenic transcription factors [36] and reduces expression of factors that inhibit myoblast transdifferentiation to adipocytes [37]. Disuse results from generalised inactivity [38], pain, or from postures and movements that shift load from the multifidus to other back muscles [39]. Disuse-mediated changes in multifidus would be more diffuse than changes caused by other mechanisms described here.

Inflammatory mechanisms

Recent work has highlighted that injury to spine structures can lead to increased expression of pro-inflammatory cytokines in multifidus [40–42]. These cytokines can cause structural changes in multifidus as observed in animal studies [40–42], and in human muscle samples [43, 44]. Pro-inflammatory cytokines have diverse biological functions and, depending on the cytokine and their interaction, can lead to muscle atrophy (e.g. tumour necrosis factor [TNF] promotes atrophy [45], protein loss [46], and muscle fibre-type transformation, leading to preferential fast fibre differentiation [47], fibrosis, and fat accumulation [48]). Inflammation-mediated muscle changes are common in other chronic diseases [46], but their association with musculoskeletal pain and injury is a recent observation [40, 44]. Cytokine expression in LBP/injury may arise from polarisation of macrophages to the pro-inflammatory M1 type [42], and the accumulation of fat, which is a potent source of cytokines [42].

Involvement of inflammatory mechanisms has important implications for the temporal and spatial features of muscle changes. Inflammatory changes can begin in the subacute period [40, 41] and become established by 6 months [40, 41]. Changes begin in a localised manner, on the side and level of injury, but then become more diffuse. Inflammatory mechanisms may occur in response to injury, develop in parallel, or even sensitise the nervous system to provoke pain [49].

Other mechanisms

Other mechanisms for changes in muscle structure are also plausible (e.g., modified afferent input from muscle spindles). More generally, spinal muscle fat accumulation and/or

atrophy occurs with ageing [50], similar to muscle changes observed throughout the body. It is critical to consider whether changes related to pain are distinct from age-related changes. Some data show independent associations of fat with pain and age [51], but not always in both sexes [52].

Implications of pathophysiology for multifidus imaging findings in LBP and injury

These various proposed pathophysiological mechanisms have implications for the timing, distribution, and nature of muscle changes studied in relation to common spinal disorders. Differences in the time course and spatial distributions of muscle changes between pathologies and individuals imply that there is unlikely to be a single imaging-based biomarker of muscle change for all patients with different pain phenotypes/spinal disorders.

As mechanisms for muscle changes are time-dependent (Table 1), *what* changes are observed (atrophy, fat accumulation, connective tissue changes) and *where* changes are observed (localised, diffuse, unilateral) depending on *when* images are acquired and the primary *mechanism* mediating changes for the individual (Fig. 1). In acute LBP, muscle atrophy (reduced muscle cross-sectional area (CSA)) may be observed at a single level on one side [14, 15], but this would involve multiple segments with denervation [15]. If the acute episode is superimposed on ongoing recurring symptoms, changes could be more diffuse or less apparent [53].

In subacute LBP, muscle size may be unaffected (after resolution of inhibition/denervation), but structural changes may be characterised by increased fat CSA [54]. In chronic LBP, changes can be diffuse, characterised by fat accumulation and muscle atrophy. However, this may differ between individuals because of differences in typical postures and movement, which may influence use/disuse.

A major issue that impacts variability of results is that most chronic LBP cases are considered to be "non-specific" without a diagnosis [55]. Within this group, there will be a variety of mechanisms (each may have unique features and distribution of muscle change), variety of spinal levels involved, and variation in time course, which will all impact the muscle imaging findings. Not surprisingly, meta-analyses of imaging studies using patients with non-specific LBP revealed inconsistent results between studies for paraspinal muscle CSA and composition [3, 4]. When the underlying location/level expressing pathology is unclear, average paraspinal muscle CSA and composition measurements acquired for the entire lumbar spine (L1-S1) have been used. This has revealed associations with IVD degeneration and Modic changes [51, 56]. Given the uncertain pathophysiology of non-specific LBP, studies should include paraspinal muscle measurements for both whole spine and an individual spinal level, if possible.

Rehabilitative exercise training and imaging-based measures of paraspinal muscles

Effects of paraspinal muscles training on image-based measures might depend on the timing, the underlying mechanism, and the structural feature being targeted. Acute atrophy has a different mechanism to chronic atrophy. Gentle precise activation of multifidus appeared sufficient to overcome acute inhibition and restore muscle CSA in one study [57], but in another did not restore muscle CSA when structural changes had developed over years [58]. In chronic LBP, initial training to ensure muscle engagement followed by application of principles of muscle overload for hypertrophy induces recovery [58]. This is supported by work that showed increased CSA of multifidus and erector spinae when training of motor control was combined with resistance training, but only erector spinae CSA increased when resistance was used without training of muscle activation patterns/motor control [59]. Cardiovascular fitness training has not been found to increase multifidus CSA [60].

Animal studies show that whole body physical activity reduces muscle inflammatory changes [61] and fibrosis, but not completely [62]. In other tissues, short-term exercise stimulates collagen synthesis and degradation to assist remodelling [63], and long-term exercise prevents ageing-dependent fibrosis [64]. This anti-fibrotic effect may be partly explained by exercise-induced reduction of inflammation [65].

Some early studies of muscle fat estimated from computed tomography (CT) showed reduction with resistance training [66]. Magnetic resonance imaging (MRI) of cervical spine muscles showed changes in proportion of fat and muscle, but it was unclear whether this was explained by greater muscle or less fat [67].

Most training studies have not considered temporal and spatial differences with pathology/pathophysiology, which makes interpretation difficult. As interpretation of imaging-based muscle measures in exercise studies will depend on the timing, underlying mechanisms and tissues targeted, this must be considered and recorded.

Potential Confounders For Interpretation Of Imaging-Based Measures Of Paraspinal Muscles

Conflicting evidence from separate clinical studies cloud an association between LBP and paraspinal muscle imaging findings [1, 3, 4]. Variation in study samples and confounding factors might explain many of these differences.

Individual-specific physiologic factors

Age- and sex-related effects on imaging-based measures of paraspinal muscles are well established [51, 68–70]. Age-induced muscle atrophy (sarcopenia) creates a time-dependent natural decline in muscle CSA and fat infiltration of paraspinal muscle [71]. Compared to males, females have more paraspinal fat and smaller muscle CSA [68] and may have greater fat infiltration in relation to spinal pathology when compared with sex-matched controls [50]. Age and sex need to be equally represented in study groups or statistically adjusted to mitigate confounding.

Body fat or body mass index does not consistently associate with higher paraspinal fat infiltration [52, 69, 72], and its role as a possible confounder of the relation between common spinal disorders and paraspinal muscle measurements is unclear. In contrast, greater aerobic fitness and physical activity levels associate with better paraspinal muscle quality (less fat infiltration) [73, 74]. This is an important consideration in studies of chronic LBP and paraspinal muscle given the negative effects of pain and disability on physical activity. Experimentally, paraspinal muscle activity has been reduced by prolonged bed rest (inactivity) or spaceflight (reduced axial loading, but maintained physical activity), with an associated reduction in paraspinal muscle CSA, increased fat content, and a possible relationship with LBP [34, 75, 76]. Although the exposure to loading and physical activity can be challenging to assess, these issues should be considered as a possible confounder.

Spinal pathology and symptoms

Imaging features of paraspinal muscle health are expected to vary with underlying spinal pathology, specific symptoms (e.g., sciatica), and associated disability. Thus, consideration should be given to co-existing spinal pathology and symptoms as possible confounders depending on the study question or relation of interest.

Consistent with the underlying role of denervation in some muscle changes, paraspinal muscle changes have been associated with specific neurocompressive spinal conditions, such as IVD herniation [21, 77], spinal stenosis [78–80], spondylolisthesis [81], and facet osteoarthritis [82]. Yet, meta-analyses of imaging studies reveal inconsistent changes in muscle CSA and note that variability in spinal locations from which measurements were collected is problematic [1]. This coincides with the notion, described above, that denervation induces a specific pattern of muscle atrophy, and findings will be inconsistent if measurements do not capture the correct levels. More uncertainty surrounds the effect of spinal pathology that can underly non-specific (localised) LBP and the relationship with paraspinal muscle imaging phenotypes. Although numerous studies show an association between paraspinal muscle imaging phenotypes and non-specific LBP [83–85], the underlying mechanisms are unclear. Features that are considered to associate with non-specific LBP often include structural abnormalities and degeneration localised to the vertebral bodies and IVDs, including disc degeneration [51, 56], Modic changes [86], and structural endplate pathologies [87].

These findings highlight that measurement and sampling of the paraspinal muscles from imaging may need to account for the location of suspected spinal pathology and how different types of pathology may have differential effects on the global patterns of paraspinal muscle health.

Importance of characterising the asymptomatic paraspinal muscle phenotype

Characterising paraspinal muscle in healthy or asymptomatic individuals provides an important reference for findings in painful spinal conditions. Spinal degeneration worsens with age and can be present in otherwise asymptomatic individuals [88, 89]. As highlighted above, paraspinal muscles also naturally atrophy with age [69, 71]. Whether muscle changes are causally related to asymptomatic degeneration is unclear, and the co-existence of these features clouds the association between imaging-based measures of paraspinal muscles and LBP. Characterisation of the natural presentation of paraspinal muscle size and composition in asymptomatic individuals is critical to define pathological values. Muscle imaging studies rarely include asymptomatic controls (matched for confounders known to impact muscle features), and this is strongly recommended in future research.

Measurement of paraspinal muscles and implications for interpretation

Imaging modalities

Paraspinal muscle morphology (e.g. CSA) has been evaluated using ultrasound imaging (US), CT, and MRI [2, 4, 6,

90]. CT and MRI enable assessment of paraspinal muscle composition (e.g. fatty infiltration) [2, 4, 90], and US echo-intensity has been used as an indicator of intra-muscular fat and connective tissue [91, 92].

Ultrasound imaging

US is easily accessible, affordable, and enables real-time imaging, which allows for evaluation of some aspects of muscle function. US has been widely used to assess contraction of paraspinal and other trunk muscles (e.g. thickness change from rest to a contracted state) in different positions [93, 94]. US has several methodological limitations. Compared to CT and MRI, US has lower image quality/contrast and measurement reliability [95–98]. Reliable identification of muscle borders and spinal landmarks is difficult, especially for structures that are parallel to the US beam (e.g. spinous process), and in overweight or older adults [97, 98].

Computerised tomography

CT has been used to assess paraspinal muscle morphology, composition, and density. Density provides an expression of muscle degeneration reflected by the number of muscle fibres, area of muscle fibres, contractile material plus fat, and connective tissue [81]. Although this technique has good intra- and inter-rater reliability [81, 99], comparison between different CT equipment is uncertain, and the placement of regions of interest (ROI) for density measurement within the muscle remains arbitrary. Selection of ROI placements that reflect muscle tissue is difficult in patients with severe fatty infiltration. Tissue contrast and resolution for paraspinal muscle are lower in CT than MRI, which impacts reliability [100]. CT involves radiation exposure, but measures can be readily made from images collected for other purposes, enabling analysis of large population-based datasets [81].

Magnetic resonance imaging

MRI is the gold standard for examination of the integrity, size, and composition of paraspinal muscle because of its superior resolution, soft tissue contrast, visualisation of spinal landmarks, and measurement reliability [100–104]. This method has potential for automated segmentation in post-processing [105]. Measures such as MR spectroscopy can detect metabolic status and composition of paraspinal muscles [106, 107]. Although MR spectroscopy measures correlate with histological findings from muscle biopsies, the method is technically demanding, and affected by sampling error, acquisition parameters, field strength, and arbitrary ROI placement [107].

Care should be taken with comparison of results and their interpretation between studies that have employed different imaging modalities (US vs. CT vs. MRI). Few studies have examined the relationship between modalities, and outcomes differ between modalities [100, 108, 109]. Multiple issues might explain differences. For instance, variation in patient positioning used for each modality (e.g., prone vs. supine) can change lumbar spine curvature which may affect measures. Comparisons are challenged by variations in measurement techniques, software, and methods used to segment paraspinal muscle or define ROIs.

MRI assessment of paraspinal muscle composition and morphology

Qualitative schemes have been used to grade the degree of paraspinal muscle fatty infiltration using MRI [52, 110, 111]. Although intra-rater (Kappa = 0.51–0.86) [52][111] and inter-rater reliability (Kappa = 0.58–0.85) is acceptable [52, 110], their scale definitions vary (e.g. 3–5-point scales). For instance, "normal" is defined as either 0–10% of intramuscular fat or no fat, and 10–50% fat can indicate slight or moderate fat [52, 110]. The Goutallier Classification System, developed to assess rotator cuff fatty infiltration, has also been adapted to evaluate lumbar multifidus fatty infiltration [112]. Visual inspection using a grid and counting the number of points touching fat and muscle tissue showed poor-to-moderate inter-rater reliability (ICCs = 0.33–0.76) [113]. Although qualitative visual assessments are less time-consuming than quantitative measures, they lack precision, have lower reliability, and are unsatisfactory in adolescents [52].

Total muscle CSA, fat CSA, and functional CSA (FCSA, area of lean muscle mass) are among the most commonly used MRI quantitative measurements of paraspinal muscle morphology and composition. These measures involve segmentation of the muscles and segregation of the pixels representative of fat and lean tissue [2, 4, 90]. Chemical shift water and fat images (e.g. DIXON, fat-signal fraction) derived from multi-echo acquisitions provide greater delineation of muscle and fat and are the contemporary standard imaging sequence for the assessment of paraspinal muscle composition [107, 114, 115]. Fat-signal fraction ($\%FSF = (Signal_{fat}/[Signal_{water} + Signal_{Fat}] \times 100$) provides the most accurate assessment of muscle composition [114]. The alternative T1- and T2-weighted images remain widely used as they are commonly available in population-based datasets [71, 116–118]. Quantitative measures of paraspinal muscle fatty infiltration using T1- of T2-weighted images are reliable [120] and provide accurate calculation of muscle composition when compared to muscle biopsy measurements and spectroscopy [107, 119]. Analysis is most often based on a thresholding or histogram function, but the definition of "fatty infiltration" varies between studies. For example, authors define fatty infiltration as the ratio of:

FCSA/CSA [71, 117], total CSA–FCSA [121], CSA fat/total CSA [116], and signal intensity of lean muscle/signal intensity of user-defined fat ROI [122]. Such variability hinders the comparison between studies. Agreement between paraspinal muscle fatty infiltration measurements obtained from chemical shift fat and water images compared to T1- and T2-weighted images remains to be established.

Definition of the ROI for analysis of lumbar paraspinal muscles differs between studies. To facilitate the use of standardised spinal muscle measurements, recent studies have proposed manual segmentation protocols [101, 120, 123]. Definition of ROI boundaries is not straightforward and depends on the tissue that is included or excluded (Fig. 2). For instance, different methods include or exclude the fatty infiltration situated outside the epimyseal border (epimuscular fat) [50, 123] leading to a systematic difference in measures of CSA and fatty infiltration between methods. Exclusion of epimuscular fat provides an accurate assessment of muscle quality within the epimyseal borders [123]. Although muscle atrophy is often accompanied by intra-fascicular and perifascicular fatty infiltration [124], it is not yet clear whether including or excluding epimuscular fat (Fig. 2c) provides the most accurate representation of overall increase in fatty infiltration and degree of muscle atrophy.

The levels, sides (e.g., bilateral or unilateral), and location at which paraspinal muscle CSA and fatty infiltration are evaluated differ between studies, adding to measurement variability. Paraspinal muscles assessed on a single axial image have been measured at mid-disc, the superior or inferior endplate, or the middle of the vertebral body [50, 85, 117, 118]. Although measures from multiple slices and 3D volumetric-based assessment [68, 125, 126] are time-consuming, as a general recommendation, paraspinal muscle CSA and composition should be averaged between adjacent slices to reduce variance. Similarly, fatty infiltration measurements should be assessed and reported for each spinal level, as fatty infiltration assessed at a single spinal level is not representative of the entire lumbar spine musculature [51]. Potential for level-specific changes, as have been observed for muscle CSA, should be considered for specific LBP presentations. Considering the unique innervation of multifidus and variations in morphology between spinal levels, bilateral paraspinal muscle measurements should be obtained at the pathological level (e.g., mid-disc or endplate of the same level) [87], and disc level below the pathology, unless more extensive measures are warranted by the specific pathology.

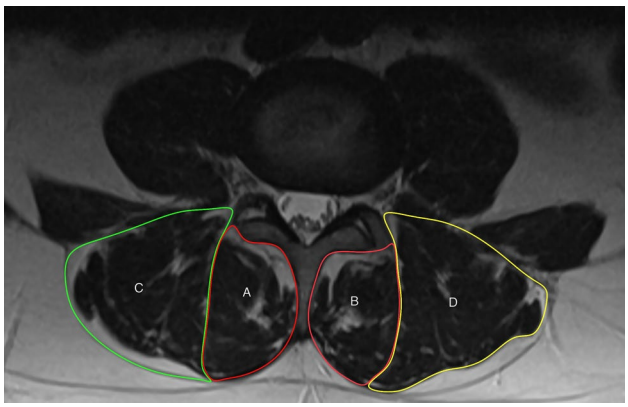

Fig. 2 Multifidus and erector spinae cross-sectional area (CSA) measurements from axial T2-weighted image. **(a)** and **(b)** the right and left CSA measurements of the multifidus muscle at the L3-L4 level. **(c)** the erector spinae CSA measurement when epimuscular fat "tent" between the muscle and facia is *included* in the ROI. **(d)** the erector spinae CSA measurement when epimuscular fat "tent" between the muscle and facia is *excluded* from the ROI

Highly reliable, quantitative MRI techniques to assess paraspinal muscle morphology and composition are time-consuming and not always feasible. Furthermore, the use of custom and proprietary image analysis software with insufficient descriptions of measurement protocols hinders replication and interpretation. Most MRI manual segmentation techniques are tedious and rater-dependent, providing an incentive for the development of automated segmentation methods. Atlas-based algorithms referenced to a standard coordinate system are well established in other domains (e.g. brain, heart) [127–130]. Development of automated algorithms likely represents the next generation of advancements in paraspinal muscle phenotyping [105].

New methods of fMRI [85] and MR elastography (MRE) [131] hold promise for characterisation of metabolic and viscoelastic properties. They may also provide non-invasive in vivo measures of paraspinal muscle function in different states (e.g., rest, contraction, stretching). New methods require validation and consideration of factors that may affect interpretation.

Recommendations towards standardisation of imaging-based measures of paraspinal muscles

Based on the issues outlined here, design of studies using image-based measures requires consideration of pathophysiology, confounders, and measurement issues to ensure

validity and interpretation of data. This would also maximise the potential to compare and combine data between studies. Recommendations for imaging-based measures of paraspinal muscles were developed and evaluated by expert consensus using a Delphi approach.

The steering committee developed 10 recommendations across the domains of "Physiology and pathophysiology", "Consideration of confounders", and "Measurement issues". The literature review and recommendations were initially evaluated in detail by three experts (Drs Dino Samartzis, Pradeep Suri, and Jeffrey Jarvik). After minor modification, recommendations were presented to the ISSLS Degenerative Spinal Phenotypes Group by the author team at the 2021 annual meeting of the International Society for the Study of the Lumbar Spine. In a first Delphi round, a survey was then sent to the 34 members of this group. The survey listed each recommendation. For each, experts could indicate whether they agreed or disagreed with the recommendation and in each case, they could provide comments. An a priori agreement threshold was set at 80%, and only recommendations with < 80% agreement would be considered in a second Delphi round.

Twenty-six responses were received (76%). All recommendations achieved agreement of 88% or greater, and no recommendations required reassessment in a second Delphi round. The author team considered all written comments and edited the recommendations at a consensus meeting. Table 2 presents the final list of recommendations. The original and revised wording for each recommendation and the % agreement achieved using the Delphi approach are presented in Supplementary online material 1.

Table 2 Recommendations towards standardisation of imaging-based measures of back muscles

Domain	Recommendation
Physiology and pathophysiology	1. In general, because of incomplete understanding of muscle changes and variation in distribution of muscle changes between pathologies, measures should be made at all levels whenever possible
	• Measures should not be averaged across all levels, and morphological differences (e.g., fat distribution and size) that are expected between levels should be accounted for in the analysis
	• Results from measures that are only made at the same single spinal level for all participants should be interpreted with caution because muscle changes would not be expected to be uniformly represented in this localised manner except in specific circumstances (e.g., participant group selected with uniform pathology at a specific level)
	2. If pathology is *known*, and the question is related to the specific identified pathology, then measurement levels should be planned with careful consideration of the expected distribution of muscle changes
	• At minimum, paraspinal muscle measurements should be obtained at the level of pathology and the level below
	• For multi-level pathology, measurements should be obtained with respect to all relevant levels
	3. If pathology is *not known*, or not relevant to the question (e.g., investigation of non-specific low back pain), then measures should be made at all levels
	4. Dependence of muscle changes on time course requires control or stratification by time if possible
	• At minimum data should be considered separately for participants with acute vs. chronic presentations
	• Choice of control or stratification based on duration should be defended
	• It is important to note that time of onset of low back symptoms might not reflect onset of pathology
	• Results from studies that combine data for participants with low back pain of different duration should be interpreted with caution
	5. Changes may affect specific muscle fascicles within the cross-sectional image and not the whole muscle area at a spine level
Consideration of confounders	1. Features that potentially influence measures require consideration
	• Features known to influence measures should be controlled analytically or by design, including age, sex
	• Features that might influence measures that should also be considered include body composition (e.g., body mass index), physical activity, pathology (if known)
	2. Measures made to quantify the effect of exercise training need to consider the expected nature and distribution of muscle changes with respect to the exercise modality and would generally involve measurement of all levels
	3. In the absence of reference data, imaging studies of clinical groups should consider (depending on the question) inclusion of control groups of participants without the condition with consideration of the potential confounders known to impact muscle features

Table 2 (continued)

Domain	Recommendation
Measurement issues	1. Description of region of interest must be included—explicit description of boundaries (include/exclude fat areas, etc.) and referenced to standard if possible
	2. Measure should differentiate fat and muscle if important for the question
	3. Magnetic resonance imaging (MRI) is the modality of choice to assess paraspinal muscle morphology. Chemical shift MRI including multi-echo acquisition is the contemporary standard for assessment of paraspinal muscle composition in human clinical studies
	4. Quantitative measurements are preferable to qualitative or semi-qualitative measurements for the assessment of paraspinal muscle composition
	5. T1- and T2-weighted MR images remain widely used clinically and provide valuable information but should be interpreted with caution. If used, and depending on the research question, reporting ratio measurements of functional cross-sectional area (where all intra-muscular fat should be excluded) to total cross-sectional area (CSA) are preferable, as they may account for inter-individual variations in anatomy and imaging parameters
	6. A common variation in segmentation of multifidus and erector spinae is to include or exclude the posterior fat band often present deep to the thoracolumbar fascia. As it is not yet clear which measure provides the most meaningful region of interest for assessment of overall fatty infiltration and related atrophy, it is recommended that studies should explicitly record whether it was included or not and consistently apply the decision across a dataset
	7. Using multiple slices and 3D-volumetric-based assessment is favoured to accurately quantify overall muscle morphology
	8. MRI slice orientation is best controlled during data collection especially at the lower lumbar levels, but correction might be required in post-processing
	9. Body position should be standardised (or documented) as changes in spinal curvature modify muscle shape/size
	10. Key imaging parameters (e.g., slice thickness, field of view, Tesla, etc.) should be clearly documented

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00586-021-06990-2.

Acknowledgements This work was supported by the Degenerative Spinal Phenotypes Group of the International Society for the Study of the Lumbar Spine (ISSLS) and was ratified by the Group after the 2021 ISSLS Annual Meeting. We thank Drs Dino Samartzis, Pradeep Suri, and Jeffrey Jarvik for detailed review of the manuscript.

Authors' contributions All authors contributed to conceptualisation of the paper and preparation of the manuscript. All authors approved the final version.

Funding PH is supported by a Fellowship from the National Health and Medical Research Council of Australia (APP1194937).

Availability of data and material All data are presented in the paper.

References

1. Cooley JR, Walker BF, Ardakani M E et al (2018) Relationships between paraspinal muscle morphology and neurocompressive conditions of the lumbar spine: a systematic review with meta-analysis. BMC Musculoskelet Disord 19:351. https://doi.org/10.1186/s12891-018-2266-5
2. Goubert D, Oosterwijck JV, Meeus M, Danneels L (2016) Structural changes of lumbar muscles in non-specific low back pain: a systematic review. Pain Physician 19:E985–E1000
3. Kalichman L, Carmeli E, Been E (2017) The Association between Imaging Parameters of the Paraspinal Muscles, Spinal Degeneration, and Low Back Pain. Biomed Res Int 2017:2562957. https://doi.org/10.1155/2017/2562957
4. Ranger TA, Cicuttini FM, Jensen TS et al (2017) Are the size and composition of the paraspinal muscles associated with low back pain? A systematic review. Spine J 17:1729–1748. https://doi.org/10.1016/j.spinee.2017.07.002
5. Rummens S, Robben E, De Groef A et al (2020) Factors associated with the ultrasound characteristics of the lumbar multifidus: A systematic review. PMR 12:82–100. https://doi.org/10.1002/pmrj.12212
6. Cuellar WA, Wilson A, Blizzard CL et al (2017) The assessment of abdominal and multifidus muscles and their role in physical function in older adults: a systematic review. Physiother 103:21–39. https://doi.org/10.1016/j.physio.2016.06.001
7. Crawford RJ, Volken T, Ni Mhuiris Á et al (2019) Geography of lumbar paravertebral muscle fatty infiltration: the influence of demographics, low back pain, and disability. Spine 44:1294–1302. https://doi.org/10.1097/BRS.0000000000003060
8. Macintosh JE, Bogduk N (1987) 1987 Volvo award in basic science. The morphology of the lumbar erector spinae. Spine 12:658–668

9. Ekholm J, Eklund G, Skoglund S (1960) On the reflex effects from the knee joint of the cat. Acta Physiol Scand 50:167–174. https://doi.org/10.1111/j.1748-1716.1960.tb02087.x
10. Lundberg A, Malmgren K, Schomburg ED (1978) Role of joint afferents in motor control exemplified by effects on reflex pathways from Ib afferents. J Physiol (Lond) 284:327–343. https://doi.org/10.1113/jphysiol.1978.sp012543
11. Stokes M, Young A (1984) The contribution of reflex inhibition to arthrogenous muscle weakness. Clin Sci 67:7–14. https://doi.org/10.1042/cs0670007
12. Iles JF, Stokes M, Young A (1990) Reflex actions of knee joint afferents during contraction of the human quadriceps. Clin Physiol 10:489–500. https://doi.org/10.1111/j.1475-097x.1990.tb00828.x
13. Hodges PW, Galea MP, Holm S, Holm AK (2009) Corticomotor excitability of back muscles is affected by intervertebral disc lesion in pigs. Eur J Neurosci 29:1490–1500. https://doi.org/10.1111/j.1460-9568.2009.06670.x
14. Hides JA, Stokes MJ, Saide M et al (1994) Evidence of lumbar multifidus muscle wasting ipsilateral to symptoms in patients with acute/subacute low back pain. Spine 19:165–172
15. Hodges P, Holm AK, Hansson T, Holm S (2006) Rapid atrophy of the lumbar multifidus follows experimental disc or nerve root injury. Spine 31:2926–2933. https://doi.org/10.1097/01.brs.0000248453.51165.0b
16. Haig AJ, Tong HC, Yamakawa KSJ et al (2005) The sensitivity and specificity of electrodiagnostic testing for the clinical syndrome of lumbar spinal stenosis. Spine 30:2667–2676. https://doi.org/10.1097/01.brs.0000188400.11490.5f
17. Haig AJ (1997) Clinical experience with paraspinal mapping. I: Neurophysiology of the paraspinal muscles in various spinal disorders. Arch Phys Med Rehabil 78:1177–1184. https://doi.org/10.1016/s0003-9993(97)90328-2
18. Haig AJ, LeBreck DB, Powley SG (1995) Paraspinal mapping. Quantified needle electromyography of the paraspinal muscles in persons without low back pain. Spine 20:715–721
19. Dulor JP, Cambon B, Vigneron P et al (1998) Expression of specific white adipose tissue genes in denervation-induced skeletal muscle fatty degeneration. FEBS Lett 439:89–92. https://doi.org/10.1016/s0014-5793(98)01216-2
20. Haig AJ (2002) Paraspinal denervation and the spinal degenerative cascade. Spine J 2:372–380. https://doi.org/10.1016/S1529-9430(02)00201-2
21. Yoshihara K, Shirai Y, Nakayama Y et al (2001) Histochemical changes in the multifidus muscle in patients with lumbar intervertebral disc herniation. Spine 26(6):622–626. https://doi.org/10.1097/00007632-200103150-00012
22. Beeler S, Ek ETH, Gerber C (2013) A comparative analysis of fatty infiltration and muscle atrophy in patients with chronic rotator cuff tears and suprascapular neuropathy. J Shoulder Elbow Surg 22:1537–1546. https://doi.org/10.1016/j.jse.2013.01.028
23. Danneels LA, Coorevits PL, Cools AM et al (2002) Differences in electromyographic activity in the multifidus muscle and the iliocostalis lumborum between healthy subjects and patients with sub-acute and chronic low back pain. Eur Spine J 11:13–19. https://doi.org/10.1007/s005860100314
24. MacDonald D, Moseley GL, Hodges PW (2009) Why do some patients keep hurting their back? Evidence of ongoing back muscle dysfunction during remission from recurrent back pain. Pain 142:183–188. https://doi.org/10.1016/j.pain.2008.12.002
25. Dankaerts W, O'Sullivan P, Burnett A, Straker L (2006) Differences in sitting postures are associated with nonspecific chronic low back pain disorders when patients are subclassified. Spine 31:698–704. https://doi.org/10.1097/01.brs.0000202532.76925.d2
26. Elgueta-Cancino E, Schabrun S, Hodges P (2018) Is the organization of the primary motor cortex in low back pain related to pain, movement, and/or sensation? Clin J Pain 34:207–216. https://doi.org/10.1097/AJP.0000000000000535
27. Tsao H, Danneels LA, Hodges PW (2011) ISSLS prize winner: smudging the motor brain in young adults with recurrent low back pain. Spine 36:1721–1727. https://doi.org/10.1097/BRS.0b013e31821c4267
28. Massé-Alarie H, Beaulieu L-D, Preuss R, Schneider C (2016) Corticomotor control of lumbar multifidus muscles is impaired in chronic low back pain: concurrent evidence from ultrasound imaging and double-pulse transcranial magnetic stimulation. Exp Brain Res 234:1033–1045. https://doi.org/10.1007/s00221-015-4528-x
29. Kiesel KB, Butler RJ, Duckworth A et al (2012) Experimentally induced pain alters the EMG activity of the lumbar multifidus in asymptomatic subjects. Man Ther 17:236–240. https://doi.org/10.1016/j.math.2012.01.008
30. Hodges PW, Moseley GL, Gabrielsson A, Gandevia SC (2003) Experimental muscle pain changes feedforward postural responses of the trunk muscles. Exp Brain Res 151:262–271. https://doi.org/10.1007/s00221-003-1457-x
31. van Dieën JH, Selen LPJ, Cholewicki J (2003) Trunk muscle activation in low-back pain patients, an analysis of the literature. J Electromyogr Kinesiol 13:333–351. https://doi.org/10.1016/S1050-6411(03)00041-5
32. Riley DA, Bain JLW, Romatowski JG, Fitts RH (2005) Skeletal muscle fiber atrophy: altered thin filament density changes slow fiber force and shortening velocity. Am J Physiol Cell Physiol 288:C360–C365. https://doi.org/10.1152/ajpcell.00386.2004
33. Hides JA, Belavý DL, Stanton W et al (2007) Magnetic resonance imaging assessment of trunk muscles during prolonged bed rest. Spine 32:1687–1692. https://doi.org/10.1097/BRS.0b013e318074c386
34. Bailey JF, Miller SL, Khieu K et al (2018) From the international space station to the clinic: how prolonged unloading may disrupt lumbar spine stability. Spine J 18:7–14. https://doi.org/10.1016/j.spinee.2017.08.261
35. Gerber C, Meyer DC, Schneeberger AG et al (2004) Effect of tendon release and delayed repair on the structure of the muscles of the rotator cuff: an experimental study in sheep. J Bone Joint Surg Am 86:1973–1982. https://doi.org/10.2106/00004623-200409000-00016
36. Kim HM, Galatz LM, Lim C et al (2012) The effect of tear size and nerve injury on rotator cuff muscle fatty degeneration in a rodent animal model. J Shoulder Elbow Surg 21:847–858. https://doi.org/10.1016/j.jse.2011.05.004
37. Akimoto T, Ushida T, Miyaki S et al (2005) Mechanical stretch inhibits myoblast-to-adipocyte differentiation through Wnt signaling. Biochem Biophys Res Commun 329:381–385. https://doi.org/10.1016/j.bbrc.2005.01.136
38. Alston W, Carlson KE, Feldman DJ et al (1966) A quantitative study of muscle factors in the chronic low back syndrome. J Am Geriatr Soc 14:1041–1047. https://doi.org/10.1111/j.1532-5415.1966.tb02885.x
39. Claus AP, Hides JA, Moseley GL, Hodges PW (2009) Different ways to balance the spine: subtle changes in sagittal spinal curves affect regional muscle activity. Spine 34:E208–E214. https://doi.org/10.1097/BRS.0b013e3181908ead
40. Hodges PW, James G, Blomster L et al (2014) Can pro-inflammatory cytokine gene expression explain multifidus muscle fiber changes after an intervertebral disc lesion? Spine 39:1010–1017
41. Hodges PW, James G, Blomster L et al (2015) Multifidus muscle changes after back injury are characterized by structural remodeling of muscle, adipose and connective tissue, but not

muscle atrophy: molecular and morphological evidence. Spine 40:1057–1071. https://doi.org/10.1097/BRS.0000000000000972
42. James G, Sluka KA, Blomster L et al (2018) Macrophage polarization contributes to local inflammation and structural change in the multifidus muscle after intervertebral disc injury. Eur Spine J 27:1744–1756. https://doi.org/10.1007/s00586-018-5652-7
43. James G, Chen X, Diwan A, Hodges PW (2020) Fat infiltration in the multifidus muscle is related to inflammatory cytokine expression in the muscle and epidural adipose tissue in individuals undergoing surgery for intervertebral disc herniation. Eur Spine J 30(4):837–845. https://doi.org/10.1007/s00586-020-06514-4
44. Shahidi B, Hubbard JC, Gibbons MC et al (2017) Lumbar multifidus muscle degenerates in individuals with chronic degenerative lumbar spine pathology. J Orthop Res 35:2700–2706. https://doi.org/10.1002/jor.23597
45. Kuru S, Inukai A, Kato T et al (2003) Expression of tumor necrosis factor-alpha in regenerating muscle fibers in inflammatory and non-inflammatory myopathies. Acta Neuropathol 105:217–224. https://doi.org/10.1007/s00401-002-0635-4
46. Li YP, Schwartz RJ, Waddell ID et al (1998) Skeletal muscle myocytes undergo protein loss and reactive oxygen-mediated NF-kappaB activation in response to tumor necrosis factor alpha. FASEB J 12:871–880. https://doi.org/10.1096/fasebj.12.10.871
47. Li YP, Schwartz RJ (2001) TNF-alpha regulates early differentiation of C2C12 myoblasts in an autocrine fashion. FASEB J 15:1413–1415. https://doi.org/10.1096/fj.00-0632fje
48. Joshi SK, Liu X, Samagh SP et al (2013) mTOR regulates fatty infiltration through SREBP-1 and PPARγ after a combined massive rotator cuff tear and suprascapular nerve injury in rats. J Orthop Res 31:724–730. https://doi.org/10.1002/jor.22254
49. Schäfers M, Sorkin LS, Sommer C (2003) Intramuscular injection of tumor necrosis factor-alpha induces muscle hyperalgesia in rats. Pain 104:579–588. https://doi.org/10.1016/s0304-3959(03)00115-5
50. Shahidi B, Parra CL, Berry DB et al (2017) Contribution of lumbar spine pathology and age to paraspinal muscle size and fatty infiltration. Spine 42:616–623. https://doi.org/10.1097/BRS.0000000000001848
51. Urrutia J, Besa P, Lobos D et al (2018) Lumbar paraspinal muscle fat infiltration is independently associated with sex, age, and inter-vertebral disc degeneration in symptomatic patients. Skeletal Radiol 47:955–961. https://doi.org/10.1007/s00256-018-2880-1
52. Kjaer P, Bendix T, Sorensen JS et al (2007) Are MRI-defined fat infiltrations in the multifidus muscles associated with low back pain? BMC Med 5:2. https://doi.org/10.1186/1741-7015-5-2
53. Danneels L, Cagnie B, D'hooge R et al (2016) The effect of experimental low back pain on lumbar muscle activity in people with a history of clinical low back pain: a muscle functional MRI study. J Neurophysiol 115:851–857. https://doi.org/10.1152/jn.00192.2015
54. Battié MC, Niemelainen R, Gibbons LE, Dhillon S (2012) Is level- and side-specific multifidus asymmetry a marker for lumbar disc pathology? Spine J 12:932–939. https://doi.org/10.1016/j.spinee.2012.08.020
55. Deyo RA, Weinstein JN (2001) Low back pain. NEJM 344(5):363–370. https://doi.org/10.1056/NEJM200102013440508
56. Teichtahl AJ, Urquhart DM, Wang Y, et al. (2016) Lumbar disc degeneration is associated with modic change and high paraspinal fat content - a 3.0T magnetic resonance imaging study. BMC Musculoskelet Disord 17:439. doi: https://doi.org/10.1186/s12891-016-1297-z
57. Hides JA, Richardson CA, Jull GA (1996) Multifidus muscle recovery is not automatic after resolution of acute, first-episode low back pain. Spine 21:2763–2769
58. Danneels LA, Vanderstraeten GG, Cambier DC et al (2001) Effects of three different training modalities on the cross sectional area of the lumbar multifidus muscle in patients with chronic low back pain. Br J Sports Med 35:186–191. https://doi.org/10.1136/bjsm.35.3.186
59. Kim J, Gong W, Hwang B (2011) The effects of resistivity and stability-combined exercise for lumbar muscles on strength, cross- sectional area and balance ability: exercises for prevention of lower back pain. J Phys Ther Sci 23:247–250
60. Shahtahmassebi B, Hebert JJ, Stomski NJ et al (2014) The effect of exercise training on lower trunk muscle morphology. Sports Med 44:1439–1458. https://doi.org/10.1007/s40279-014-0213-7
61. James G, Millecamps M, Stone LS, Hodges PW (2018) Dysregulation of the Inflammatory Mediators in the Multifidus Muscle After Spontaneous Intervertebral Disc Degeneration SPARC-null Mice is Ameliorated by Physical Activity. Spine 43:E1184–E1194. https://doi.org/10.1097/BRS.0000000000002656
62. James G, Klyne DM, Millecamps M et al (2019) ISSLS Prize in Basic science 2019: physical activity attenuates fibrotic alterations to the multifidus muscle associated with intervertebral disc degeneration. Eur Spine J 28:893–904. https://doi.org/10.1007/s00586-019-05902-9
63. Miller BF, Olesen JL, Hansen M et al (2005) Coordinated collagen and muscle protein synthesis in human patella tendon and quadriceps muscle after exercise. J Physiol (Lond) 567:1021–1033. https://doi.org/10.1113/jphysiol.2005.093690
64. Astrom M-B, Feigh M, Pedersen BK (2010) Persistent low-grade inflammation and regular exercise. Front Biosci (Schol Ed) 2:96–105. https://doi.org/10.2741/s48
65. Gleeson M, Bishop NC, Stensel DJ et al (2011) The anti-inflammatory effects of exercise: mechanisms and implications for the prevention and treatment of disease. Nat Rev Immunol 11:607–615. https://doi.org/10.1038/nri3041
66. Mayer J, Mooney V, Dagenais S (2008) Evidence-informed management of chronic low back pain with lumbar extensor strengthening exercises. Spine J 8:96–113. https://doi.org/10.1016/j.spinee.2007.09.008
67. O'leary S, Jull G, Van Wyk L, et al (2015) Morphological changes in the cervical muscles of women with chronic whiplash can be modified with exercise-A pilot study. Muscle Nerve 52:772–779. https://doi.org/10.1002/mus.24612
68. Crawford RJ, Filli L, Elliott JM et al (2016) Age- and level-dependence of fatty infiltration in lumbar paravertebral muscles of healthy volunteers. AJNR Am J Neuroradiol 37:742–748. https://doi.org/10.3174/ajnr.A4596
69. Dahlqvist JR, Vissing CR, Hedermann G et al (2017) Fat replacement of paraspinal muscles with aging in healthy adults. Med Sci Sports Exerc 49:595–601. https://doi.org/10.1249/MSS.0000000000001119
70. Johannesdottir F, Allaire B, Anderson DE et al (2018) Population-based study of age- and sex-related differences in muscle density and size in thoracic and lumbar spine: the Framingham study. Osteoporos Int 29:1569–1580. https://doi.org/10.1007/s00198-018-4490-0
71. Fortin M, Videman T, Gibbons LE, Battié MC (2014) Paraspinal muscle morphology and composition: a 15-yr longitudinal magnetic resonance imaging study. Med Sci Sports Exerc 46:893–901. https://doi.org/10.1249/MSS.0000000000000179
72. Parkkola R, Kormano M (1992) Lumbar disc and back muscle degeneration on MRI: correlation to age and body mass. J Spinal Disord 5:86–92
73. Prasarn ML, Kostantinos V, Coyne E et al (2015) Does lumbar paraspinal muscle fatty degeneration correlate with aerobic index

and Oswestry disability index? Surg Neurol Int 6:S240–S243. https://doi.org/10.4103/2152-7806.156606
74. Teichtahl AJ, Urquhart DM, Wang Y et al (2015) Physical inactivity is associated with narrower lumbar intervertebral discs, high fat content of paraspinal muscles and low back pain and disability. Arthritis Res Ther 17:114. https://doi.org/10.1186/s13075-015-0629-y
75. Belavý DL, Armbrecht G, Richardson CA et al (2011) Muscle atrophy and changes in spinal morphology: is the lumbar spine vulnerable after prolonged bed-rest? Spine 36:137–145. https://doi.org/10.1097/BRS.0b013e3181cc93e8
76. Chang DG, Healey RM, Snyder AJ et al (2016) Lumbar spine paraspinal muscle and intervertebral disc height changes in astronauts after long-duration spaceflight on the international space station. Spine 41:1917–1924. https://doi.org/10.1097/BRS.0000000000001873
77. Fortin M, Lazáry À, Varga PP et al (2016) Paraspinal muscle asymmetry and fat infiltration in patients with symptomatic disc herniation. Eur Spine J 25:1452–1459. https://doi.org/10.1007/s00586-016-4503-7
78. Abbas J, Slon V, May H et al (2016) Paraspinal muscles density: a marker for degenerative lumbar spinal stenosis? BMC Musculoskelet Disord 17:422. https://doi.org/10.1186/s12891-016-1282-6
79. Fortin M, Lazáry À, Varga PP, Battié MC (2017) Association between paraspinal muscle morphology, clinical symptoms and functional status in patients with lumbar spinal stenosis. Eur Spine J 26:2543–2551. https://doi.org/10.1007/s00586-017-5228-y
80. Jiang J, Wang H, Wang L et al (2017) Multifidus degeneration, a new risk factor for lumbar spinal stenosis: a case-control study. World Neurosurg 99:226–231. https://doi.org/10.1016/j.wneu.2016.11.142
81. Kalichman L, Hodges P, Li L et al (2010) Changes in paraspinal muscles and their association with low back pain and spinal degeneration: CT study. Eur Spine J 19:1136–1144. https://doi.org/10.1007/s00586-009-1257-5
82. Yu B, Jiang K, Li X et al (2017) Correlation of the features of the lumbar multifidus muscle with facet joint osteoarthritis. Orthopedics 40:e793–e800. https://doi.org/10.3928/01477447-20170531-05
83. Danneels LA, Vanderstraeten GG, Cambier DC et al (2000) CT imaging of trunk muscles in chronic low back pain patients and healthy control subjects. Eur Spine J 9:266–272. https://doi.org/10.1007/s005860000190
84. Hides J, Gilmore C, Stanton W, Bohlscheid E (2008) Multifidus size and symmetry among chronic LBP and healthy asymptomatic subjects. Man Ther 13:43–49. https://doi.org/10.1016/j.math.2006.07.017
85. Goubert D, De Pauw R, Meeus M et al (2017) Lumbar muscle structure and function in chronic versus recurrent low back pain: a cross-sectional study. Spine J 17:1285–1296. https://doi.org/10.1016/j.spinee.2017.04.025
86. Teichtahl AJ, Urquhart DM, Wang Y et al (2015) Fat infiltration of paraspinal muscles is associated with low back pain, disability, and structural abnormalities in community-based adults. Spine J 15:1593–1601. https://doi.org/10.1016/j.spinee.2015.03.039
87. Bailey JF, Fields AJ, Ballatori A et al (2019) The relationship between endplate pathology and patient-reported symptoms for chronic low back pain depends on lumbar paraspinal muscle quality. Spine 44:1010–1017. https://doi.org/10.1097/BRS.0000000000003035
88. Brinjikji W, Luetmer PH, Comstock B et al (2015) Systematic literature review of imaging features of spinal degeneration in asymptomatic populations. AJNR Am J Neuroradiol 36:811–816. https://doi.org/10.3174/ajnr.A4173
89. Crawford RJ, Volken T, Valentin S et al (2016) Rate of lumbar paravertebral muscle fat infiltration versus spinal degeneration in asymptomatic populations: an age-aggregated cross-sectional simulation study. Scoliosis Spinal Disord 11:21. https://doi.org/10.1186/s13013-016-0080-0
90. Suri P, Fry AL, Gellhorn AC (2015) Do muscle characteristics on lumbar spine magnetic resonance imaging or computed tomography predict future low back pain, physical function, or performance? a systematic review. PM R 7:1269–1281. https://doi.org/10.1016/j.pmrj.2015.04.016
91. Masaki M, Ikezoe T, Fukumoto Y et al (2016) Association of walking speed with sagittal spinal alignment, muscle thickness, and echo intensity of lumbar back muscles in middle-aged and elderly women. Aging Clin Exp Res 28:429–434. https://doi.org/10.1007/s40520-015-0442-0
92. Yoshiko A, Kaji T, Sugiyama H et al (2018) Muscle quality characteristics of muscles in the thigh, upper arm and lower back in elderly men and women. Eur J Appl Physiol 118:1385–1395. https://doi.org/10.1007/s00421-018-3870-7
93. Lee S, Chan CK, Lam T et al (2006) Relationship between low back pain and lumbar multifidus size at different postures. Spine 31:2258–2262. https://doi.org/10.1097/01.brs.0000232807.76033.33
94. Sweeney N, O'Sullivan C, Kelly G (2014) Multifidus muscle size and percentage thickness changes among patients with unilateral chronic low back pain (CLBP) and healthy controls in prone and standing. Man Ther 19:433–439. https://doi.org/10.1016/j.math.2014.04.009
95. Stokes M, Rankin G, Newham DJ (2005) Ultrasound imaging of lumbar multifidus muscle: normal reference ranges for measurements and practical guidance on the technique. Man Ther 10:116–126. https://doi.org/10.1016/j.math.2004.08.013
96. Pressler JF, Heiss DG, Buford JA, Chidley JV (2006) Between-day repeatability and symmetry of multifidus cross-sectional area measured using ultrasound imaging. J Orthop Sports Phys Ther 36:10–18. https://doi.org/10.2519/jospt.2006.36.1.10
97. Cuellar WA, Blizzard L, Callisaya ML et al (2017) Test-retest reliability of measurements of abdominal and multifidus muscles using ultrasound imaging in adults aged 50–79 years. Musculoskelet Sci Pract 28:79–84. https://doi.org/10.1016/j.msksp.2016.11.013
98. Wilson A, Hides JA, Blizzard L et al (2016) Measuring ultrasound images of abdominal and lumbar multifidus muscles in older adults: A reliability study. Man Ther 23:114–119. https://doi.org/10.1016/j.math.2016.01.004
99. Kalichman L, Klindukhov A, Li L, Linov L (2016) Indices of paraspinal muscles degeneration: reliability and association with facet joint osteoarthritis: feasibility study. Clin Spine Surg 29(9):465–470
100. Hu Z-J, He J, Zhao F-D et al (2011) An assessment of the intra- and inter-reliability of the lumbar paraspinal muscle parameters using CT scan and magnetic resonance imaging. Spine 36:E868–E874. https://doi.org/10.1097/BRS.0b013e3181ef6b51
101. Fortin M, Battié MC (2012) Quantitative paraspinal muscle measurements: inter-software reliability and agreement using OsiriX and ImageJ. Phys Ther 92:853–864. https://doi.org/10.2522/ptj.20110380
102. Sasaki T, Yoshimura N, Hashizume H et al (2017) MRI-defined paraspinal muscle morphology in Japanese population: the Wakayama Spine study. PLoS ONE 12:e0187765. https://doi.org/10.1371/journal.pone.0187765
103. Paalanne N, Niinimäki J, Karppinen J et al (2011) Assessment of association between low back pain and paraspinal muscle atrophy using opposed-phase magnetic resonance imaging: a

population-based study among young adults. Spine 36:1961–1968. https://doi.org/10.1097/BRS.0b013e3181fef890
104. Ranson CA, Burnett AF, Kerslake R et al (2006) An investigation into the use of MR imaging to determine the functional cross sectional area of lumbar paraspinal muscles. Eur Spine J 15:764–773. https://doi.org/10.1007/s00586-005-0909-3
105. Xiao Y, Fortin M, Battié MC, Rivaz H (2018) Population-averaged MRI atlases for automated image processing and assessments of lumbar paraspinal muscles. Eur Spine J 27:2442–2448. https://doi.org/10.1007/s00586-018-5704-z
106. Mengiardi B, Schmid MR, Boos N et al (2006) Fat content of lumbar paraspinal muscles in patients with chronic low back pain and in asymptomatic volunteers: quantification with MR spectroscopy. Radiol 240:786–792. https://doi.org/10.1148/radiol.2403050820
107. Fischer MA, Nanz D, Shimakawa A et al (2013) Quantification of muscle fat in patients with low back pain: comparison of multi-echo MR imaging with single-voxel MR spectroscopy. Radiol 266:555–563. https://doi.org/10.1148/radiol.12120399
108. Hides JA, Richardson CA, Jull GA (1995) Magnetic resonance imaging and ultrasonography of the lumbar multifidus muscle. Comparison of two different modalities Spine 20(1):54–58. https://doi.org/10.1097/00007632-199501000-00010
109. Belavý DL, Armbrecht G, Felsenberg D (2015) Real-time ultrasound measures of lumbar erector spinae and multifidus: reliability and comparison to magnetic resonance imaging. Physiol Meas 36:2285–2299. https://doi.org/10.1088/0967-3334/36/11/2285
110. Kader DF, Wardlaw D, Smith FW (2000) Correlation between the MRI changes in the lumbar multifidus muscles and leg pain. Clin Radiol 55:145–149. https://doi.org/10.1053/crad.1999.0340
111. Ropponen A, Videman T, Battié MC (2008) The reliability of paraspinal muscles composition measurements using routine spine MRI and their association with back function. Man Ther 13:349–356. https://doi.org/10.1016/j.math.2007.03.004
112. Battaglia PJ, Maeda Y, Welk A et al (2014) Reliability of the Goutallier classification in quantifying muscle fatty degeneration in the lumbar multifidus using magnetic resonance imaging. J Manipulative Physiol Ther 37:190–197. https://doi.org/10.1016/j.jmpt.2013.12.010
113. Bhadresha A, Lawrence OJ, McCarthy MJH (2016) A comparison of magnetic resonance imaging muscle fat content in the lumbar paraspinal muscles with patient-reported outcome measures in patients with lumbar degenerative disk disease and focal disk prolapse. Global Spine J 6:401–410. https://doi.org/10.1055/s-0036-1583290
114. Yoo YH, Kim H-S, Lee YH et al (2015) Comparison of multi-echo dixon methods with volume interpolated breath-hold gradient echo magnetic resonance imaging in fat-signal fraction quantification of paravertebral muscle. Korean J Radiol 16:1086–1095. https://doi.org/10.3348/kjr.2015.16.5.1086
115. Reeder SB, Hu HH, Sirlin CB (2012) Proton density fat-fraction: a standardized mr-based biomarker of tissue fat concentration. J Magn Reson Imaging 36:1011–1014. https://doi.org/10.1002/jmri.23741
116. Hebert JJ, Kjaer P, Fritz JM, Walker BF (2014) The relationship of lumbar multifidus muscle morphology to previous, current, and future low back pain: a 9-year population-based prospective cohort study. Spine 39:1417–1425. https://doi.org/10.1097/BRS.0000000000000424
117. Fortin M, Gibbons LE, Videman T, Battié MC (2015) Do variations in paraspinal muscle morphology and composition predict low back pain in men? Scand J Med Sci Sports 25:880–887. https://doi.org/10.1111/sms.12301
118. Mhuiris ÁN, Volken T, Elliott JM et al (2016) Reliability of quantifying the spatial distribution of fatty infiltration in lumbar paravertebral muscles using a new segmentation method for T1-weighted MRI. BMC Musculoskelet Disord 17:234. https://doi.org/10.1186/s12891-016-1090-z
119. Gaeta M, Scribano E, Mileto A et al (2011) Muscle fat fraction in neuromuscular disorders: dual-echo dual-flip-angle spoiled gradient-recalled MR imaging technique for quantification–a feasibility study. Radiology 259:487–494. https://doi.org/10.1148/radiol.10101108
120. Crawford RJ, Cornwall J, Abbott R, Elliott JM (2017) Manually defining regions of interest when quantifying paravertebral muscles fatty infiltration from axial magnetic resonance imaging: a proposed method for the lumbar spine with anatomical cross-reference. BMC Musculoskelet Disord 18:25. https://doi.org/10.1186/s12891-016-1378-z
121. Pezolato A, de Vasconcelos EE, Defino HLA, Nogueira-Barbosa MH (2012) Fat infiltration in the lumbar multifidus and erector spinae muscles in subjects with sway-back posture. Eur Spine J 21:2158–2164. https://doi.org/10.1007/s00586-012-2286-z
122. D'hooge R, Cagnie B, Crombez G et al (2012) Increased intramuscular fatty infiltration without differences in lumbar muscle cross-sectional area during remission of unilateral recurrent low back pain. Man Ther 17:584–588. https://doi.org/10.1016/j.math.2012.06.007
123. Berry DB, Padwal J, Johnson S et al (2018) Methodological considerations in region of interest definitions for paraspinal muscles in axial MRIs of the lumbar spine. BMC Musculoskelet Disord 19:135. https://doi.org/10.1186/s12891-018-2059-x
124. Gibbons MC, Singh A, Anakwenze O et al (2017) Histological evidence of muscle degeneration in advanced human rotator cuff disease. J Bone Joint Surg Am 99:190–199. https://doi.org/10.2106/JBJS.16.00335
125. Valentin S, Yeates TD, Licka T, Elliott J (2015) Inter-rater reliability of trunk muscle morphometric analysis. J Back Musculoskelet Rehabil 28:181–190. https://doi.org/10.3233/BMR-140552
126. Valentin S, Licka T, Elliott J (2015) Age and side-related morphometric MRI evaluation of trunk muscles in people without back pain. Man Ther 20:90–95. https://doi.org/10.1016/j.math.2014.07.007
127. Kazemifar S, Drozd JJ, Rajakumar N et al (2014) Automated algorithm to measure changes in medial temporal lobe volume in Alzheimer disease. J Neurosci Methods 227:35–46. https://doi.org/10.1016/j.jneumeth.2014.01.033
128. Mikheev A, Nevsky G, Govindan S et al (2008) Fully automatic segmentation of the brain from T1-weighted MRI using bridge burner algorithm. J Magn Reson Imaging 27:1235–1241. https://doi.org/10.1002/jmri.21372
129. Shahzad R, Bos D, Budde RPJ et al (2017) Automatic segmentation and quantification of the cardiac structures from non-contrast-enhanced cardiac CT scans. Phys Med Biol 62:3798–3813. https://doi.org/10.1088/1361-6560/aa63cb
130. Depa M, Sabuncu MR, Holmvang G et al (2010) Robust atlas-based segmentation of highly variable anatomy: left atrium segmentation. Stat Atlases Comput Models Heart 6364:85–94. https://doi.org/10.1007/978-3-642-15835-3_9
131. Creze M, Soubeyrand M, Yue JL et al (2018) Magnetic resonance elastography of the lumbar back muscles: a preliminary study. Clin Anat 31:514–520. https://doi.org/10.1002/ca.23065